TRANSFORMATION OF CHRONIC MYELOGENOUS LEUKEMIA TO MULTIPLE MYELOMA: A CASE REPORT

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Abstract- Chronic myelogenous leukemia (CML) is a stem cell disorder sometimes associated with lymphoproliferative disorders. CML may precede a lymphoproliferative disorder. There are a few reports showing associations of CML with multiple myeloma and we report a known CML case that transformed into a full-blown multiple myeloma. This patient had more than 69% of infiltrating myeloma cells in her bone marrow and Philadelphia chromosome was detected in 18 out of 42. However, the probable presence of some myeloma cells with classic Philadelphia-positive chromosome could be proposed.

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Key Words: Leukemia, myeloid, chronic, multiple myeloma, cell transformation, neoplastic, Philadelphia chromosome

INTRODUCTION

Chronic Myelogenous Leukemia (CML) results from the malignant transformation of a single stem cell. It may involve erythropoiesis, neutrophilopoiesis, eosinophilopoiesis, basophilopoiesis, monocytopoiesis and thrombopoiesis in chronic phase of CML, with presence of Philadelphia (Ph) chromosome (22q-) in erythroblasts, neutrophilic, eosinophilic and basophilic granulocytes, macrophages and megakaryocytes. Several observations suggest that some lymphocytes may be derived from the primordial malignant cell. Also it appears that phenotypically normal B-lymphocytes are derived from the malignant clone, placing the primary leukemogenic process closer to, if not, in the pleuripotential stem cell (1,2). In most cases of CML, the patient's chronic disease eventually changes to a more aggressive disease. Usually this transformation is towards acute myelogenous leukemia or acute lymphoblastic leukemia. Cytogenetic evidence indicates that the accelerated phase of the disease results from a progressive change in the clone that supports the chronic phase. Often chromosomal abnormalities occur in addition to Ph chromosome, but the Ph chromosome persists, marking the more disturbed hematopoiesis as being generated from the old but now even more abnormal and disordered clone.

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In this report we present a patient with chronic myelogenous leukemia with transformation to Ph-positive multiple myeloma.

CASE REPORT

A 64-year-old female who showed signs of epigastric discomfort, mild splenomegaly and leukocytosis, was referred to our center in September 1991 (Table 1).

Table 1. Laboratory results

	Chronic phase	Myeloma phase
WBC /µl	65100	31900
Lymphocyte	18%	18%
Neutrophil	69%	68%
Metamyelocyte	2%	10%
Myelocyte	5%	-
Basophile	5%	-
Eosinophil	-	2%
Blast	1%	-
Hb (g/ml)	11.6	7.9
Plt /µl	405000	125000
BUN (mg/dl)	-	36
Creatinin (mg/dl)	-	3.9
Uric acid (mg/dl)	-	11
Serum Pr. Electrophoresis	-	
Alb (g/l)		3
Gamma region (g/l)	-	6.7

Bone marrow study indicated CML and was confirmed by cytogenetic investigation and the presence of Ph-positive chromosome (Fig. 1). Treatment started with busulfan and changed to hydroxyurea two years later.

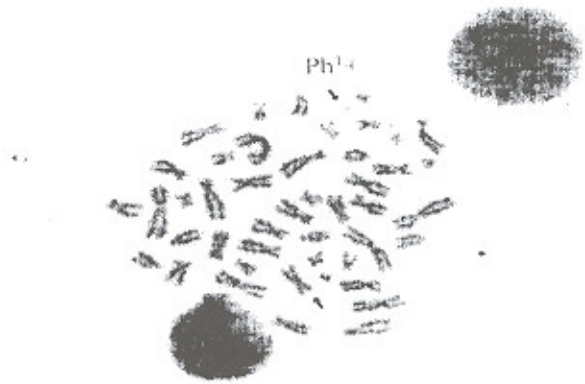
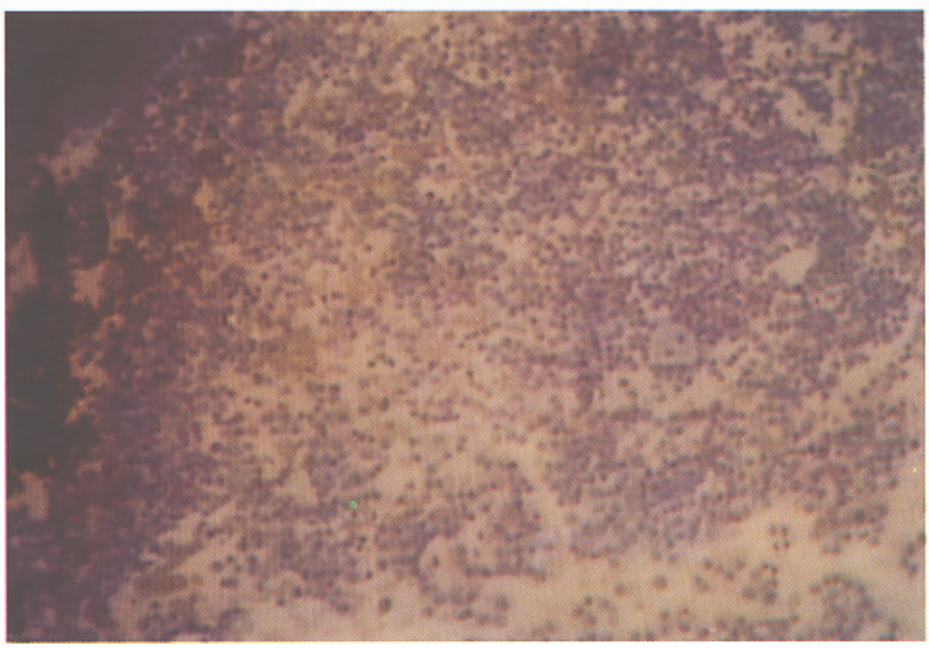
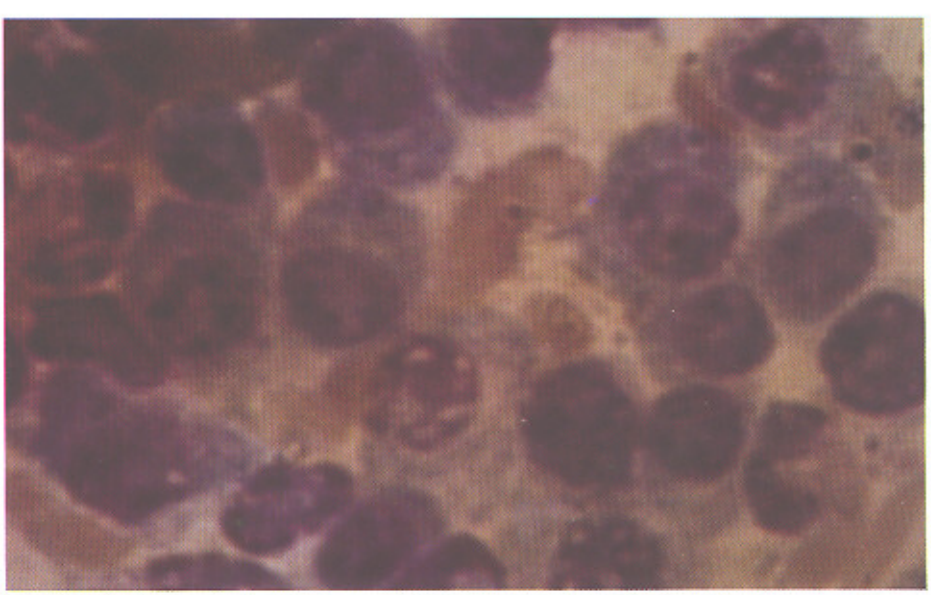


Fig. 1. The presence of Philadelphia-positive chromosome was shown by karyotype study

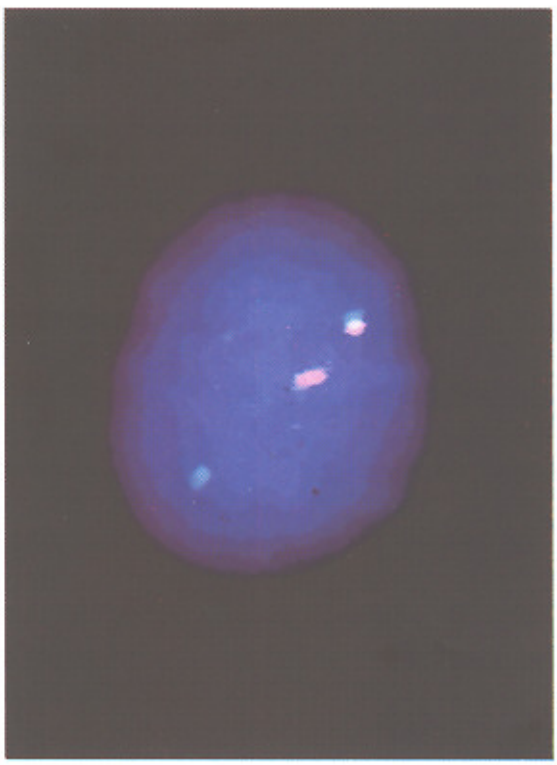


(a)

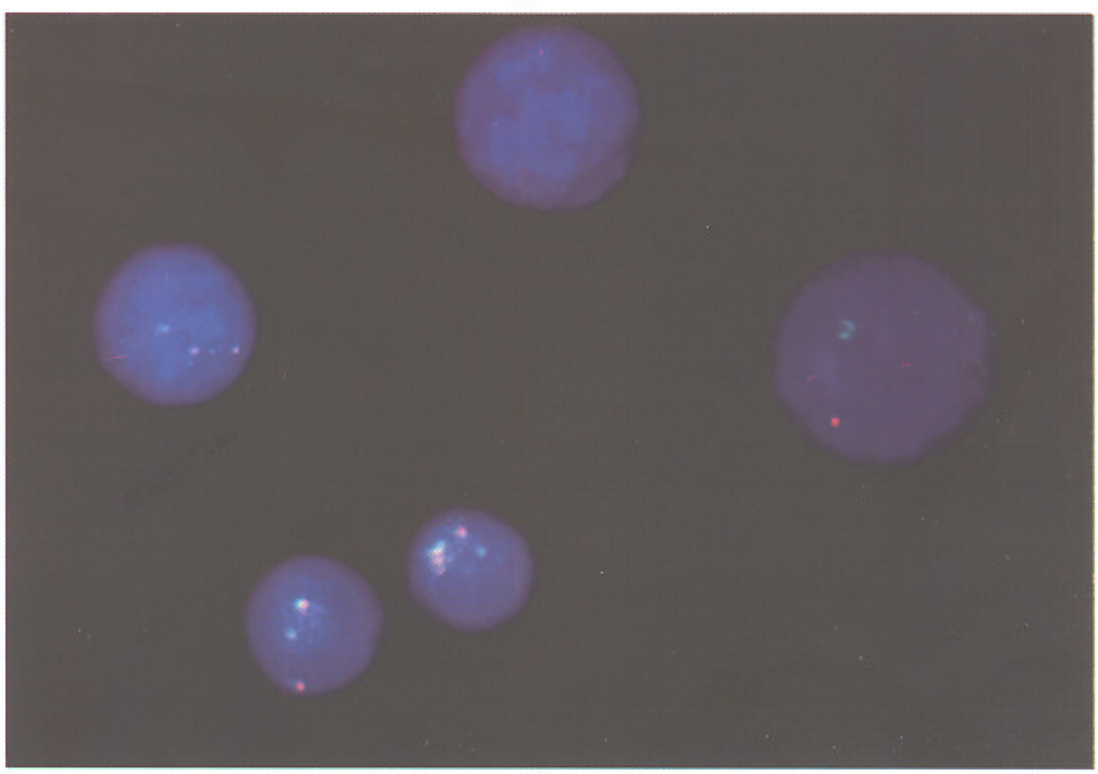


(b)

Fig. 2. Hypercellular marrow (85% cellularity) with 65% myeloma cells infiltrating the bone marrow (a×100, b×1000)



(a)



(b)

Fig. 3. These photos show nuclei reveal with only 3 hybridization signals in each nucleus. Two of these signals, one green and one red, were normally expressed, that means, one was localized on chromosome 9 and one on chromosome 22. The third signal was a hybrid composed of the overlap of a green and a red signal. It proves that a translocation 9/22 had occurred.

She had no problem till December 1997, when she developed palor and fever. Physical examination revealed neither organomegaly nor lymphadenopathy, although primary evaluation showed leukocytosis, anemia and renal failure (Table 1). The blood culture was negative but the urine culture was positive for *Staphilococcus aureous* and then renal function deteriorated progressively. Her bone marrow study revealed a hypercellular marrow (85% cellularity) with 65% myeloma cells infiltrating the bone marrow (Fig. 2).

The serum protein electrophoresis showed a sharp dense band in gamma region but her skull radiography was normal and no lytic bone lesion was seen. Cytogenetic and FISH study of the bone marrow that was heavily infiltrated by myeloma cells showed Ph-positive chromosome (Fig. 3). Dialysis, antibiotic and chemotherapy began but she died due to renal failure and sepsis 15 days later.

DISCUSSION

CML is a stem cell disorder and is associated with lymphoproliferation. CML may precede a lymphoproliferative disorder and some patients may have concurrent lymphoproliferative or plasmacytic malignancies and CML. Lymphoma or lymphoblastic leukemia (3-6), essential monoclonal gammopathy (7, 8), myeloma (9-11) or Waldenström macroglobulinemia (12) could occur in association with CML.

Both Cλ gene locus and bcr translocation breakpoint are located in the chromosome 22q11 band. The classical λ chain locus (composed of the centric Vλ gene and Cλ 1-6 exons) is not involved in the translocation and remains on chromosome 22. The bcr and λ genes are separated by at least 100 kb. Accordingly the Cλ genes retain a germ line configuration in the leukemic cells (11) and multiple myeloma.

This case cannot be explained by a variant translocation process, which could directly involve the λ locus. In contrast to previous reports (11) we had enriched plasma cell preparation and we could demonstrate that B-cell clone producing the monoclonal immuno-globuline might carry the Ph chromosome.

Dedication

Dedicated to the late Dr. Peyman Nasseri.

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